

Substitute form 1449A/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet 1 of 1

Complete if Known

Application Number	10/075,097
Filing Date	02/13/2002
First Named Inventor	Nnochiri N. Ekwuribe
Group Art Unit	1654
Examiner Name	Anish Gupta
Attorney Docket Number	9233-46

JAN 23 2004

O I P E J C S T  
PATENT & TRADEMARK OFFICE**U.S. PATENTS AND PATENT PUBLICATIONS**

Examiner Initials*	Cite No.	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY
		Number	Kind Code (if known)		
ADL	1	US-5,889,153		Suzuki et al.	03/30/1999

**OTHER NON PATENT LITERATURE DOCUMENTS**

Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T
ADL	2	Aoki et al. "Chronic Intermittent Intravenous Insulin Therapy: A New Frontier in Diabetes Therapy" <i>Diabetes Technology &amp; Therapeutics</i> 3(1):111-123 (2001)	
	3	Clement, Stephen "A Dose-Escalation Study of the Effects of Two Sequential Doses of Oral Modified Insulin on Blood Glucose Concentrations in Patients with Type 1 Diabetes Mellitus" American Diabetes Association Annual Meeting (June 25, 2001) (Poster)	
	4	Francis et al. "Polyethylene Glycol Modification: Relevance of Improved Methodology to Tumour Targeting" <i>Journal of Drug Targeting</i> 3:321-340 (1996)	
	5	Guzman et al. "Effects of Fatty Ethers and Stearic Acid on the Gastrointestinal Absorption of Insulin" <i>PRHSJ</i> 9(2):155-159 (1990)	
	6	International Search Report, PCT/US02/04440, 12/23/2003	
	7	Lindsay et al. <i>The Acetylation of Insulin Biochem J.</i> 121:737-745 (1971)	
	8	Liu et al. "Glucose-Induced Release of Glycosylpoly(ethylene glycol) Insulin Bound to a Soluble Conjugate of Concanavalin A" <i>Bioconjugate Chem.</i> 8:664-672 (1997)	
	9	Mesiha et al. "Hypoglycaemic effect of oral insulin preparations containing Brij 35, 52, 58 or 92 and stearic acid" <i>J. Pharm. Pharmacol.</i> 33:733-734 (1981)	
	10	Michael et al. "Loss of Insulin Signaling in Hepatocytes Leads to Severe Insulin Resistance and Progressive Hepatic Dysfunction" <i>Molecular Cell</i> 6:87-97 (1999)	
	11	Moghaddam, Amir "Use of polyethylene glycol polymers for bioconjugations and drug development" <i>American Biotechnology Laboratory</i> pp. 42, 44 (July 2001)	
	12	Neubauer et al. "Influence of Polyethylene Glycol Insulin on Lipid Tissues of Experimental Animals" <i>Diabetes</i> 32:953-958 (October 1983)	
	13	Puskas et al. "Investigation of Chymotrypsin Digestion Profile of Orally Active Insulin Conjugate Him2" <i>AAPS PharmSci</i> 3(3) (2001) (Abstract)	
	14	Radakrishnan et al. "Stability and Physical Characteristics of Orally Active Amphiphilic Human Insulin Analog, Methoxy (Polyethylene Glycol) Hexanoyl Human Recombinant Insulin (HIM2)" <i>Proceed. Int'l. Symp. Control. Rel. Bioact. Mater.</i> 27:1038-39 (2000)	
	15	Shen et al. "(C) Means to Enhance Penetration; (3) Enhancement of polypeptide and protein absorption by macromolecular carriers via endocytosis and transcytosis" <i>Advanced Drug Del. Reviews</i> 8:93-113 (1992)	
	16	Sindelar et al. "A Comparison of the Effects of Selective Increases in Peripheral or Portal Insulin on Hepatic Glucose Production in the Conscious Dog" <i>Diabetes</i> 45:1594-1604 (1996)	
	17	Sirokman et al. "Refolding and proton pumping activity of a polyethylene glycol-bacteriorhodopsin water-soluble conjugate" <i>Protein Science</i> 12:1161-1170 (1993)	
	18	Torchilin, Vladimir P. "Immunoliposomes and PEGylated Immunoliposomes: Possible Use for Targeted Delivery of Imaging Agents" <i>Immunomethods</i> 4:244-258 (1994)	
	19	Wei et al. "A Poly(Ethylene Glycol) Water-soluble Conjugate of Porin: Refolding to the Native State" <i>Biochemistry</i> 34:6408-6415 (1995)	
	20	Xia et al. "Effects of polyoxyethylene chain length distribution on the interfacial properties of polyethylene glycol n-dodecyl ether" <i>Yingyong Huaxue</i> 2(4): 59-65 (1985) (Abstract)	
ADL	21	Zalipsky et al. "Peptide Attachment to Extremities of Liposomal Surface Grafted PEG Chains: Preparation of the Long-Circulating Form of Laminin Pentapeptide YIGSR" <i>Bioconjugate Chem.</i> 6:705-708 (1995)	

Examiner Signature

Date Considered

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449 U.S. Department of Commerce  
Patent and Trademark Office

Attorney Docket Number  
9233-46

Serial No.  
10/075,097

LIST OF DOCUMENTS CITED BY APPLICANT

(Use several sheets if necessary)

Applicants: Ekwuribe et al.

Filing Date  
February 13, 2002

Group  
1646

U. S. PATENT DOCUMENTS

Examiner Initial		Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
ADK	1.	2002/0160938	10/31/2002	Brandenburg et al.	A1		
ADK	2.	2003/0144468	07/31/2003	Ekwuribe et al.	A1		
	3.	2003/0087808	05/08/2003	Soltero et al.	A1		
	4.	2003/0083232	05/01/2003	Soltero et al.	A1		
ADK	5.	2003/0069170	04/10/2003	Soltero et al.	A1		
ADK	6.	2003/0060606	03/27/2003	Ekwuribe et al.	A1		
	7.	2003/0050228	03/13/2003	Ekwuribe et al.	A1		
ADK	8.	2003/0027995	02/06/2003	Ekwuribe et al.	A1		
ADK	9.	2003/0004304	01/02/2003	Ekwuribe et al.	A1		
	10.	4,602,043	07/22/1986	Geho			
	11.	4,662,872	05/05/1987	Cané			
	12.	4,704,394	11/03/1987	Geho			
	13.	4,761,287	08/02/1988	Geho			
	14.	4,822,337	04/18/1989	Newhouse et al.			
	15.	4,863,896	09/05/1989	Geho et al.			
	16.	4,963,526	10/16/1990	Ecanow			
	17.	5,320,094	06/14/1994	Laube et al.	A		
	18.	5,321,009	06/14/1994	Baeder et al.	A		
	19.	5,364,838	11/15/1994	Rubsamen	A		
	20.	5,420,108	05/30/1995	Shohet	A		
	21.	5,468,727	11/21/1995	Phillips et al.	A		
	22.	5,597,797	01/28/1997	Clark et al.	A		
ADK	23.	5,681,567	10/28/1997	Martinez et al.	A		

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LIST OF DOCUMENTS CITED BY APPLICANT							
(Use several sheets if necessary)							
Applicants: Ekwuribe et al.							
Filing Date February 13, 2002						Group 1654 1646	
ADK	24.	5,704,910	01/06/1998	Humes	A		
↑	25.	5,714,519	02/03/1998	Cincotta et al.	A		
	26.	5,763,396	06/09/1998	Weiner et al.	A		
	27.	5,843,866	12/01/1998	Weiner et al.	A		
	28.	5,866,584	02/02/1999	Cincotta et al.	A		
	29.	5,997,848	12/07/1999	Patton et al.	A		
	30.	6,042,822	03/28/2000	Gilbert et al.	A		
	31.	6,057,292	05/02/2000	Cunningham et al.	A		
	32.	6,147,108	11/14/2000	Hauptman	A		
↓	33.	6,342,225	01/29/2002	Jones et al.	B1		
ADK	34.	6,506,730	01/14/2003	Lee et al.	B1		
FOREIGN PATENT DOCUMENTS							
1		Document Number	Date	Country	Class	Subclass	Translation Yes   No
	35.	EP 0 511 903	10/14/1998	EP	B1		Claims
	36.	99/65941	12/23/1999	WO	A1		
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)							
ADK	37.	Agarwal et al. "Polymethacrylate-based Microparticulates of Insulin for Oral Delivery: Preparation and In Vitro Dissolution Stability in the Presence of Enzyme Inhibitors" <i>International Journal of Pharmaceutics</i> 225:31-39 (2001)					
↑	38.	Allaudeen et al. "Orally Active Insulin: A Single Insulin Conjugate Selected for Future Studies" 60 <sup>th</sup> Annual Meeting of the American Diabetes Assoc., Atlanta, GA June 2000 (Abstract)					
	39.	Anderson et al. "HIM2, a Novel Modified Insulin, has Improved Systemic Pharmacokinetics in Normal Dogs, Compared to Unmodified Insulin" <i>American Diabetes Association 62<sup>nd</sup> Annual Meeting June 2002 (Abstract)</i>					
	40.	Block, Lawrence H. "Pharmaceutical Emulsions and Microemulsions" <i>Pharmaceutical Dosage Forms: Disperse Systems</i> , Vol. 2, Ed. Lieberman et al. (1996) p 47-109.					
↓	41.	Bone et al. "Successful Treatment of an Insulin Dependent Rat Model of Human Type I Diabetes with Orally Active Insulin" Program and Abstracts, 4 <sup>th</sup> International Workshop on Lessons from Animal Diabetes, Omiya, Japan November 1994 (Abstract)					
ADK	42.	Bone et al. "Successful Treatment of Type I Diabetes with Orally-Active Insulin: Studies in The Insulin Dependent BB/S Rat" Program and Abstracts, 55 <sup>th</sup> Annual Meeting of the American Diabetes Association, Atlanta Georgia, June 1995 (Abstract)					

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<b>FORM PTO-1449 U.S. Department of Commerce</b> Patent and Trademark Office		Attorney Docket Number 9233-46	Serial No. 10/075,097
<b>LIST OF DOCUMENTS CITED BY APPLICANT</b> (Use several sheets if necessary)			
OIPE JCT09 NOV 26 2003 PATENT & TRADEMARK OFFICE		Applicants: Ekwuribe et al.	
		Filing Date February 13, 2002	Group 1654 <del>1648</del>
43.	Brange and Volund "Insulin Analogs with Improved Pharmacokinetic Profiles" <i>Advanced Drug Delivery Reviews</i> 35:307-335 (1999)		
44.	Cleland et al. "Emerging Protein Delivery Methods" <i>Current Opinion in Biotechnology</i> 12:212-219 (2001)		
45.	Clement et al. "Effects of Multiple Doses of Orally Administered Hexyl Insulin M2 (HIM2) on Postprandial Blood Glucose (PPG) Concentrations in Type 1 Diabetic (T1) Patients" American Diabetes Association 62 <sup>nd</sup> Annual Meeting, June 2002 (Poster)		
46.	Clement et al. "Oral Insulin Product Hexyl-Insulin Monoconjugate 2 (HIM2) in Type 1 Diabetes Mellitus: The Glucose Stabilization Effects of HIM2" <i>Diabetes Technology &amp; Therapeutics</i> 4(4):459-466 (2002)		
47.	Clement, Stephen "A Dose-Escalation Study of the Effects of Two Sequential Doses of Oral Modified Insulin on Blood Glucose Concentrations in Patients with Type 1 Diabetes Mellitus" American Diabetes Association Annual Meeting (June 25, 2001) (Abstract)		
48.	Dange et al. "Poly(alkyl cyanoacrylate) Nanospheres for Oral Administration of Insulin" <i>Journal of Pharmaceutical Sciences</i> 86(12):1403-1409 (Dec. 1997)		
49.	Dandona et al. "Effect of an Oral Modified Insulin on Blood Glucose Levels in Fasting and Fed Type 1 Diabetic Patients Receiving a "Basal" Regimen of Injected Insulin" American Diabetes Association Annual Meeting (June 25, 2001) (Abstract)		
50.	Ekwuribe et al. "Calcitonin Drug-Oligomer Conjugates, and Uses Thereof" U.S. Serial No. 10/166,355, filed 11/08/2002, including Preliminary Amendment dated 02/26/2003 and Supplemental Preliminary Amendment dated 03/31/2003		
51.	Ekwuribe et al. "Mixtures of Drug-Oligomer Conjugates Comprising Polyalkylene Glycol, Uses Thereof, and Methods of Making Same" U.S. Serial No. 09/873,797, filed 06/04/2001		
52.	Ekwuribe et al. "Oral Insulin Delivery: Hydrolyzable Amphiphilic Oligomer Conjugates Prolong Glucose Reduction" <i>Proceed. Int'l. Symp. Control. Rel. Bioact. Mater.</i> 26:147-148 (1999)		
53.	Ekwuribe, Nnochiri "Conjugation-Stabilized Polypeptide Compositions, Therapeutic Delivery and Diagnostic Formulations Comprising Same, and Method of Making and Using the Same" <i>Biotechnology Advances</i> 14(4):575-576 (1996) (Abstract)		
54.	Hinds et al. "Synthesis and Characterization of Poly(ethylene glycol)-Insulin Conjugates" <i>Bioconjugate Chem.</i> 11:195-201 (2000)		
55.	Kipnes et al. "Control of Postprandial Plasma Glucose by an Oral Insulin Product (HIM2) in Patients with Type 2 Diabetes" <i>Emerging Treatments and Technologies</i> 26:2 (2003)		
56.	Kipnes et al. "The Effects of an Oral Modified Insulin on Postprandial Blood Glucose Levels in Patients with Type 2 Diabetes" American Diabetes Association Annual Meeting (June 24, 2001) (Abstract)		
57.	Kipnes et al. "The Effects of an Oral Modified Insulin on Postprandial Blood Glucose Levels in Patients with Type 2 Diabetes Mellitus" American Diabetes Association Annual Meeting (June 24, 2001) (Poster)		
58.	Kube, D.M. "Multitalented Proteins Play a Key Role in Therapeutics" <i>Genomics and Proteomics</i> (Sept. 2002)		
59.	Marschutz et al. "Oral Peptide Drug Delivery: Polymer-Inhibitor Conjugates Protecting Insulin from Enzymatic Degradation In Vitro" <i>Biomaterials</i> 21:1499-1507 (2000)		
60.	Musabayane et al. "Orally Administered, Insulin-Loaded Amidated Pectin Hydrogel Beads Sustain Plasma Concentrations of Insulin in Streptozotocin-Diabetic Rats" <i>Journal of Endocrinology</i> 164:1-6 (2000)		
61.	Pang, David C. "Bridging Gaps in Drug Discovery and Development" <i>Pharmaceutical Technology</i> 82-94 (Nov. 1998)		

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<b>LIST OF DOCUMENTS CITED BY APPLICANT</b> (Use several sheets if necessary)		Applicants: Ekwuribe et al.	
		Filing Date February 13, 2002	Group 1654 1646
		Pauletti et al. "Improvement of Oral Peptide Bioavailability: Peptidomimetics and Prodrug Strategies" <i>Advanced Drug Delivery Reviews</i> 27:235-256 (1997)	
63.		Puskas et al. "Investigation of Chymotrypsin Digestion Profile of Orally Active Insulin Conjugate HIM2" <i>AAPS Pharm. Sci.</i> 3(3) 2001 (Abstract)	
64.		Radhakrishnan et al. "Chemical Modification of Insulin with Amphiphilic Polymers Improves Intestinal Delivery" <i>Proceed. Intl. Symp. Control. Rel. Bioact. Mater.</i> 25:124-125 (1998) (Abstract)	
65.		Radhakrishnan et al. "Oral Delivery of Insulin: Single Selective Modification at B29-LYS With Amphiphilic Oligomer" Program and Abstracts, 1999 National Meeting of the Ameri. Assoc. Pharm. Scient., New Orleans, LA (1999) (Abstract)	
66.		Radhakrishnan et al. "Structure-Activity Relationship of Insulin Modified with Amphiphilic Polymers" Program and Abstracts, 1998 National Meeting of the Amer. Assoc. Pharm. Scient., San Francisco, CA <i>Pharm. Sci.</i> 1(1):S-59 (1998) (Abstract)	
67.		Radhakrishnan et al., "Insulin Polypeptide-Oligomer Conjugates, Proinsulin Polypeptide-Oligomer Conjugates and Methods of Synthesizing Same" U.S. Serial No. 10/389,499, filed 03/17/2003	
68.		Richards et al. "Self-Association Properties of Monomeric Insulin Analogs Under Formulation Conditions" <i>Pharmaceutical Research</i> 15(9):1434-1441 (1998)	
69.		Shah and Shen "Transcellular Delivery of an Insulin-Transferrin Conjugate in Enterocyte-like Caco-2 Cells" <i>Journal of Pharmaceutical Sciences</i> 85(12):1306-1311 (1996)	
70.		Sluzky et al. "Kinetics of Insulin Aggregation in Aqueous Solutions Upon Agitation in the Presence of Hydrophobic Surfaces" <i>Proc. Natl. Acad. Sci.</i> 88:9377-9381 (Nov. 1991)	
71.		Soltero et al. "Insulin Polypeptide-Oligomer Conjugates, Proinsulin Polypeptide-Oligomer Conjugates and Methods of Synthesizing Same" U.S. Serial No. 10/382,022, filed 03/05/2003	
72.		Soltero et al. "Pharmaceutical Compositions of Drug-Oligomer Conjugates and Methods of Treating Diseases Therewith" U.S. Serial No. 10/382,069, filed 03/05/2003	
73.		Soltero et al. "Pharmaceutical Compositions of Insulin Drug-Oligomer Conjugates and Methods of Treating Diseases Therewith" U.S. Serial No. 10/382,155, filed 03/05/2003	
74.		Song et al. "Direct Measurement of Pulsatile Insulin Secretion from the Portal Vein in Human Subjects" <i>Journal of Clinical Endocrinology &amp; Metabolism</i> 85(12):4491-4499 (2000)	
75.		Still and McAllister "Effects of Orally Active Modified Insulin in Type I Diabetic Patients" <i>Clinical Pharmacol. Therap.</i> 69(2): P95 (Feb. 2001) (Abstract)	
76.		Still and McAllister "Effects of Orally Active Modified Insulin in Type I Diabetic Patients" Slide Presentation 2001 Annual Meeting of the American Society for Clinical Pharmacology & Therapeutics, Orlando, FL, March 9, 2001	
77.		Still and McAllister "Effects of Orally Active Modified Insulin in Type I Diabetic Patients" 2001 Annual Meeting of the American Society for Clinical Pharmacology & Therapeutics, Orlando, FL, March 9, 2001 (Handout)	
78.		Still et al. "Magnitude and Variability of Pharmacokinetic and Glucodynamic Responses to Modified Human Insulin Administered Orally to Healthy Volunteers" <i>Diabetes Research and Clinical Practice</i> 56:S77 (2002)	
79.		Still et al. "Methods of Reducing Hypoglycemic Episodes in the Treatment of Diabetes Mellitus" U.S. Serial No. 10/461,199, filed 06/13/2003	
80.		Still, J. Gordon "Development of Oral Insulin: Progress and Current Status" <i>Diabetes/Metabolism Research and Reviews</i> , 18(1):S29-S37 (2002)	

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 \*EXAMINER

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		<b>Applicants:</b> Ekwuribe et al.	
		<b>Filing Date</b> February 13, 2002	<b>Group</b> 1650 1646
81. <i>Still, J. Gordon "Oral Insulin Development" Slide Presentation, VI International St.Barts Symposium Diabetes 2000: Therapy and Technology, London, England, May 12, 2000</i>			
82. <i>Stocklin et al. "A Stable Isotope Dilution Assay for the In Vivo Determination of Insulin Levels in Humans by Mass Spectrometry" Diabetes 46(1):1-7 (Jan. 1997)</i>			
83. <i>Tyle, Praveen "Iontophoretic Devices for Drug Delivery" Pharmaceutical Research 3(6):318-326 (1986)</i>			
84. <i>Uchio et al. "Site-Specific Insulin Conjugates with Enhanced Stability and Extended Action Profile" Advanced Drug Delivery Reviews 35:289-306 (1999)</i>			
85. <i>Vreeland et al. "Molar Mass Profiling of Synthetic Polymers by Free-Solution Capillary Electrophoresis of DNA-Polymer Conjugates" Anal. Chem. 73(8):1795-1803 (2001)</i>			
86. <i>Ziv and Bendayan "Intestinal Absorption of Peptides Through the Enterocytes" Microscopy Research and Technique 49:346-352 (2000)</i>			

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QUARTER  
JAN 13 2003  
PATENT & TRADEMARK OFFICE


U. S. PATENT DOCUMENTS							
Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate	
	1.	3,919,411	11/11/75	Glass et al.			
	2.	3,256,153	06/14/66	Heimlech			
	3.	3,868,356	02/25/75	Smyth			
	4.	3,950,517	04/13/76	Lindsay et al.			
	5.	4,003,792	01/18/77	Mill et al.			
	6.	4,044,196	08/23/77	Huper et al.			
	7.	4,087,390	05/02/78	Shields			
	8.	4,093,574	06/06/78	Shields			
	9.	4,100,117	07/11/78	Shields			
	10.	4,179,337	12/18/79	Davis et al.			
	11.	4,229,438	10/21/80	Fujino et al.			
	12.	4,253,998	03/03/81	Sarantakis			
	13.	4,277,394	07/07/81	Fujino et al.			
	14.	4,338,306	07/06/82	Kitao et al.			
	15.	4,348,387	09/07/82	Brownlee et al.			
	16.	4,410,547	10/18/83	Ueno et al.			
	17.	4,469,681	09/04/84	Brownlee et al.			
	18.	4,472,382	09/18/84	Labrie et al.			
	19.	4,554,101	11/19/85	Hopp			
	20.	4,579,730	04/01/86	Kidron et al.			
	21.	4,585,754	04/29/86	Meisner et al.			
	22.	4,622,392	11/11/86	Hong et al.			
	23.	4,684,524	08/04/87	Eckenhoff et al.			
	24.	4,698,264	10/06/87	Steinke			
	25.	4,717,566	01/05/88	Eckenhoff et al.			

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				Applicants: Ekwuribe et al.			
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<b>U.S. PATENT DOCUMENTS (CONT.)</b>							
26.	4,744,976	05/17/88	Snipes et al.				
27.	4,772,471	09/20/88	Vanlerberghe et al.				
28.	4,797,288	01/10/89	Sharma et al.				
29.	4,839,341	06/13/89	Massey et al.				
30.	4,840,799	06/20/89	Applegren et al.				
31.	4,849,405	07/18/89	Ecanow				
32.	4,917,888	04/17/90	Katre et al.				
33.	4,935,246	06/19/90	Ahrens				
34.	4,946,828	08/07/90	Markussen				
35.	4,957,910	09/18/90	Sutton et al.				
36.	4,963,367	10/16/90	Ecanow				
37.	4,994,439	02/19/91	Longenecker et al.				
38.	5,013,556	05/07/91	Woodle et al.				
39.	5,055,300	10/08/91	Gupta				
40.	5,055,304	10/08/91	Makino et al.				
41.	5,089,261	02/18/92	Nitecki et al.				
42.	5,093,198	03/03/92	Speaker et al.				
43.	5,157,021	10/20/92	Balschmidt et al.				
44.	5,162,430	11/10/92	Rhee et al.				
45.	5,164,366	11/17/92	Balschmidt et al.				
46.	5,202,415	04/13/93	Jonassen et al.				
47.	5,206,219	04/27/93	Desai				
48.	5,283,236	02/01/94	Chiou				
49.	5,286,637	02/15/94	Veronese et al.				
50.	5,292,802	03/08/94	Rhee et al.				
51.	5,304,473	04/19/94	Belagaje et al.				
52.	5,308,889	05/03/94	Rhee et al.				
53.	5,312,808	05/17/94	Shorr et al.				

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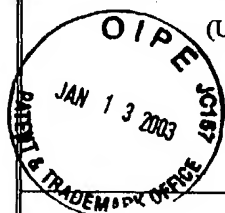
FORM PTO-1449 U.S. Department of Commerce  
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Attorney Docket Number  
9233-46

Serial No.  
10/075,097

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Applicants:

Ekwuribe et al.

Filing Date: 02/13/02

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1646

U.S. PATENT DOCUMENTS (CONT.)

1654

ADK	54.	5,324,775	06/28/94	Rhee et al.			
↑	55.	5,328,955	07/12/94	Rhee et al.			
	56.	5,359,030	10/25/94	Ekwuribe			
	57.	5,405,621	04/11/95	Sipos			
	58.	5,405,877	04/11/95	Greenwald et al			
	59.	5,413,791	05/09/95	Rhee et al.			
	60.	5,415,872	05/16/95	Sipos			
	61.	5,438,040	08/01/95	Ekwuribe			
	62.	5,444,041	08/22/95	Owen et al.			
	63.	5,446,091	08/29/95	Rhee et al.			
	64.	5,457,066	10/10/95	Frank et al.			
	65.	5,461,031	10/24/95	De Felippis			
	66.	5,468,478	11/21/95	Saifer et al.			
	67.	5,504,188	04/02/96	Baker et al.			
	68.	5,506,203	04/09/96	Backstrom et al.			
	69.	5,518,998	05/21/96	Backstrom et al.			
	70.	5,523,348	06/04/96	Rhee et al.			
	71.	5,529,915	06/25/96	Phillips et al.			
	72.	5,550,188	08/27/96	Rhee et al.			
	73.	5,545,618	08/13/96	Buckley et al.			
	74.	5,567,422	10/22/96	Greenwald			
	75.	5,606,038	02/25/97	Regen			
	76.	5,612,460	03/18/97	Zalipsky			
	77.	5,631,347	05/20/97	Baker et al.			
	78.	5,637,749	06/10/97	Greenwald			
	79.	5,646,242	07/08/97	Baker et al.			
	80.	5,650,388	07/22/97	Shorr et al.			
ADK	81.	5,658,878	08/19/97	Backstrom et al.			

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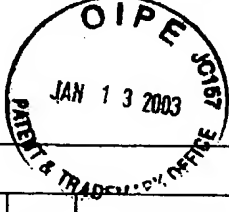
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<b>LIST OF DOCUMENTS CITED BY APPLICANT</b> <div style="display: flex; align-items: center; justify-content: center; margin-top: 10px;"> <div style="border: 1px solid black; border-radius: 50%; padding: 10px; text-align: center; margin-right: 10px;">             (Use several sheets if necessary)  <b>JAN 13 2003</b>              PATENT &amp; TRADEMARK OFFICE           </div> </div>							
				Applicants: Ekwuribe et al.			
				Filing Date: 02/13/02		Group 1646	
<b>U.S. PATENT DOCUMENTS (CONT.)</b>							
1654							
	82.	5,681,567	10/28/97	Baker et al.			
ADK	83.	5,681,811	10/28/97	Ekwuribe			
	84.	5,693,609	12/02/97	Baker et al.			
	85.	5,693,769	12/02/97	Kahne et al.			
	86.	5,700,904	12/23/97	Baker et al.			
	87.	5,707,648	01/13/98	Yiv			
	88.	5,738,846	04/14/98	Greenwald et al.			
	89.	5,747,445	05/05/98	Backstrom et al.			
	90.	5,747,642	05/05/98	De Felippis			
	91.	5,750,497	05/12/98	Havelund et al.			
	92.	5,766,620	06/16/98	Heiber et al.			
	93.	5,824,638	10/20/98	Burnside et al.			
	94.	5,830,853	11/03/98	Backstrom et al.			
	95.	5,830,918	11/03/98	Sportsman et al.			
	96.	5,849,860	12/15/98	Hakimi et al.			
	97.	5,853,748	12/29/98	New			
	98.	5,854,208	12/29/98	Jones et al.			
	99.	5,856,451	01/05/99	Olsen et al.			
	100.	5,866,538	02/02/99	Norup et al.			
	101.	5,874,111	02/23/99	Maitra et al.			
	102.	5,898,028	04/27/99	Jensen et al.			
	103.	5,902,588	05/11/99	Greenwald et al.			
	104.	5,905,140	05/18/99	Hansen			
	105.	5,907,030	05/25/99	Shen et al.			
	106.	5,922,675	07/13/99	Baker et al.			
	107.	5,932,462	08/03/99	Harris et al.			
ADK	108.	5,942,248	08/24/99	Barnwell			
	109.	5,948,751	09/07/99	Kimer et al.			

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				<b>Filing Date:</b> 02/13/02		<b>Group</b> 1646	
<b>U.S. PATENT DOCUMENTS (CONT.)</b>							
ADK	110.	5,952,008	09/14/99	Backstrom et al.			
↑	111.	5,952,297	09/14/99	De Felippis et al.			
	112.	5,962,267	10/05/99	Shin et al.			
	113.	5,968,549	10/19/99	New et al.			
	114.	5,969,040	10/19/99	Hallahan et al.			
	115.	5,981,709	11/09/99	Greenwald et al.			
	116.	5,985,263	11/16/99	Lee et al.			
	117.	6,004,574	12/21/99	Backstrom et al.			
	118.	6,025,325	02/15/00	Campfield et al.			
	119.	6,034,054	03/07/00	De Felippis et al.			
	120.	6,043,214	03/28/00	Jensen et al.			
	121.	6,051,551	04/18/00	Hughes et al.			
	122.	6,063,761	05/16/00	Jones et al.			
	123.	6,093,391	07/25/00	Kabanov et al.			
	124.	6,113,906	09/05/00	Greenwald et al.			
	125.	6,165,976	12/26/00	Backstrom et al.			
	126.	6,177,087	01/23/01	Greenwald et al.			
	127.	6,191,105	02/20/01	Ekwuribe et al.			
	128.	6,200,602	03/13/01	Watts et al.			
	129.	6,211,144	04/03/01	Havelund			
	130.	6,248,363	06/19/01	Patel et al.			
	131.	6,251,856	06/26/01	Markussen et al.			
	132.	6,258,377	07/10/01	New et al.			
	133.	6,268,335	07/31/01	Brader			
	134.	6,306,440	10/23/01	Backstrom et al.			
	135.	6,309,633	10/30/01	Ekwuribe et al.			
ADK	136.	6,310,038	10/30/01	Havelund			

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DATE CONSIDERED

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Group <del>1646</del> 1654							
U.S. PATENT DOCUMENTS (CONT.)							
	137.	6,323,311	11/27/01	Liu et al.			
	138.	6,335,316	01/01/02	Hughes et al.			
FOREIGN PATENT DOCUMENTS							
		Document Number	Date	Country	Class	Subclass	Translation Yes   No
	139.	GB 1 492 997	11/23/77	Great Britain			Yes
	140.	EP 0 031 567	07/08/81	EPO			Yes
	141.	JP 1 254 699	10/11/89	Japan			No
	142.	WO 93/01802	02/04/93	PCT			Yes - abstract
	143.	WO 95/09831	04/13/95	PCT			Yes
	144.	EP 0 483 465	08/02/95	EPO			Yes - claims
	145.	WO 95/30641	11/16/95	PCT			Yes
	146.	EP 0 597 007	10/16/96	EPO			Yes
	147.	EP 0 621 777	11/09/96	EPO			Yes - claims
	148.	WO 98/07745	02/26/98	PCT			Yes
	149.	EP 0 797 615	01/13/99	EPO			Yes
	150.	WO 99/32134	07/01/99	PCT			Yes
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)							
	151.	Abuchowski, A. and F. F. Davis, "Soluble Polymer-Enzyme Adducts," pp. 368-383, Enzymes as Drugs, J. S. Holcenberg, John Wiley, 1981.					
	152.	Akiyama, M. et al., "The Synthesis of New Derivatives of 1-.beta.-D-Arabinofuranosylcytosine," Chem. Pharm. Bull., 1978, 26(3): p. 981-984.					
	153.	Allcock et al., "Contemporary Polymer Chemistry," 394-403 (2nd. ed., 1991).					
	154.	Ansell, S. et al., "Application of Oligo-(14-amino-3,6,9,12-tetraoxatetradecanoic acid) Lipid Conjugates as Steric Barrier Molecules in Liposomal Formulations," Bioconjugate Chem., 10: 653-666 (1999).					
	155.	Aoshima, M. et al., "N-sup.4-Behenoyl-1-.beta.-D-Arabinofuranosylcytosine as a Potential New Antitumor Agent," Cancer Research, 1977, 37: pp. 2481-2486.					
	156.	Baker, D. C. et al., "Prodrugs of 9-.beta.-D-Arabinofuranosyladenine. 1. Synthesis and Evaluation of Some 5'-(O-Acyl) Derivatives," J. Med. Chem., 1978, 21(12): pp. 1218-1221.					
	157.	Banting et al., "Pancreatic Extracts in the Treatment of Diabetes Mellitus: Preliminary Report," Can. Med. Assoc. J., 145(10): 1281-1286 (1991).					
	158.	Banting, R. G., et al., "Pancreatic Extracts in the Treatment of Diabetes Mellitus," The Canadian Med. Assoc. J. 1992, 12: 141-146.					

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 \*EXAMINER

DATE CONSIDERED

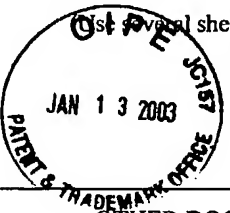
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<b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.) (CONT.)</b>			
<div style="text-align: right;">1654</div>			
159.	Baudys et al., "Stabilization and Intestinal Absorption of Human Calcitonin," J. Contr. Rel., 39: 145-51 (1996).		
160.	Baudys, M. et al., "Synthesis and Characterization of Different Glycosylated Derivatives of Insulin" Proceed. Intern. Symp. Cont. Rel. Bioactive. Mater., 1992, 19: 210-211.		
161.	Boccu, E. et al., "Pharmacokinetic Properties of Polyethylene Glycol Derivatized Superoxide Dismutase," Pharm. Res. Comm., 1982 14: 113-120.		
162.	Brange, J., "Galenics of Insulin: The Physico-Chemical and Pharmaceutical Aspects of Insulin and Insulin Preparations," Novo Research Institute, Denmark, 18-100 (1987).		
163.	Brange, J. et al., "Chemical Stability of Insulin. 1. Hydrolytic Degradation During Storage of Pharmaceutical Preparations," Pharm. Res., 1992, 9 (6): 715-726.		
164.	Brange, J. et al., "Chemical Stability of Insulin. 2. Formation of Higher Molecular Weight Transformation Products During Storage of Pharmaceutical Preparations," Pharm. Res., 1992, 9 (6) 727-734.		
165.	Chen et al., "Synthesis and Properties of AMA Amphiphiles," J. Org. Chem., 64: 6870-6873 (1999).		
166.	Chien, Y. W., Novel Drug Delivery Systems, pp. 678-679, Marcell Deffer, Inc., New York, N.Y., 1992.		
167.	Comrad, R.A., et al., "The Influence of Peptide Structure on Transport Across Caco-2 Cells," Pharm. Res., 1991, 8(12): 1453-1459.		
168.	Coombes, A.G.A. et al., "Biodegradable Polymeric Microparticles for Drug Delivery and Vaccine Formulation: the Surface Attachment of Hydrophilic Species Using the Concept of Poly(Ethylene Glycol) Anchoring Segments," Biomaterials, 18: 1153-1161 (1997).		
169.	Coudert et al., "A Novel, Unequivocal Synthesis of Polyethylene Glycols," Synthetic Communications, 16(1): 19-26 (1986).		
170.	Delgado et al., "The Uses and Properties of PEG-Linked Proteins" Critical Reviews in Therapeutic Drug Carrier Systems 9:3,4 249-304 (1992).		
171.	Engel et al., "Insulin: Intestinal Absorption as Water-in-Oil-in-Water Emulsions" NATURE 219 856-857 (1968).		
172.	Fasano, Alessio, "Innovative strategies for the oral delivery of drugs and peptides" TIBTECH 16 152-157 (1998).		
173.	Forst et al., "New Aspects on Biological Activity of C-peptide in IDDM Patients," Exp. Clin. Endocrinol. Diabetes, 106: 270-276 (1998).		
174.	Gish, D. T. et al., "Nucleic Acids. 11. Synthesis of 5' Esters of 1-beta-D-Arabinofuranosylcytosine Possessing Antileukemic and Immunosuppressive Activity," J. Med. Chem., 1971, 14(12): pp. 1159-1162.		
175.	Gombotz et al., "Biodegradable Polymers for Protein and Peptide Drug Delivery," Bioconjugate Chem., 6: 332-351 (1995).		
176.	Harris, J. Milton, "Laboratory Synthesis of Polyethylene Glycol Derivatives," I. Macromol. Science - Rev. Macromol. Chem. Phys., C25(3): 325-373 (1985).		
177.	Hashimoto et al., "Synthesis of Palmitoyl Derivatives of Insulin and Their Biological Activities," Pharmaceutical Research, 6(2): 171-176 (1989).		
178.	Hostetler, K. Y. et al., "Synthesis and Antiretroviral Activity of Phospholipid Analogs of Azidothymidine and Other Antiviral Nucleosides," The Journal of Biological Chemistry, 1990, 265(11): pp. 6112-6117.		
179.	Hong, C. I. et al., "Nucleoside Conjugates. 7. Synthesis and Antitumor Activity of 1-beta-D-Arabinofuranosylcytosine Conjugates of Ether Lipids," J. Med. Chem., 1986, 29: pp. 2038-2044.		

EXAMINER  
\*EXAMINER

DATE CONSIDERED

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1654				
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.) (CONT.)				
180.	Igarashi, R. et al, "Biologically Active Peptides Conjugated with Lecithin for DDS" Proceed. Intern. Symp. Cont. Rel. Bioactiv. Mater. 1990, 17 367-368.			
181.	Kemmler et al., "On the Nature and Subcellular Localization of the Proinsulin Converting Enzymes," Federation Proceedings, 30(Abtract 924): 1210Abs (1971).			
182.	Kemmler et al., "Studies on the Conversion of Proinsulin to Insulin: I. Conversion in Vitro with Trypsin and Carboxypeptidase B," The Journal of Biological Chemistry, 246(22) 6786-6791 (November 25, 1971).			
183.	King et al.; "Preparation of Protein Conjugates with Alkoxypolyethylene Glycols" Int. J. Peptide Protein Res. 16 147-155 (1980).			
184.	M. Maislos et al, "The Source of the Circulating Aggregate of Insulin in Type I Diabetic Patients is Therapeutic Insulin" J. Clin. Invest., 1986, 77: 717-723.			
185.	Nucci, et al. "The Therapeutic Value of Poly(ethylene Glycol)-Modified Proteins" Ac. Drug. Del. Rev. 6: 133-151 1991.			
186.	Oka, K. et al, "Enhanced Intestinal Absorption of a Hydrophobic Polymer-conjugated Protein Drug, Smaones, in an Oily Formulation" Pharm. Res., 1990, 7 (8): 852-855.			
187.	Patel et al. "Oral Administration of Insulin By Encapsulation Within Liposomes" FEBS Lett. 62(1) 60-63 1976.			
188.	Price, J.C, <i>Polyethylene Glycol</i> , 355-361.			
189.	Ratner, R. E. et al. "Persistent Cutaneous Insulin Allergy Resulting from High-Molecular Weight Insulin Aggregates," Diabetes, 1990, 39: 728-733.			
190.	Robbins, D. C. et al, "Antibodies to Covalent Aggregates of Insulin in Blood of Insulin-Using Diabetic Patients" Diabetes, 1987, 36: 838-841.			
191.	Russell-Jones, G. J. "Vitamin B12 Drug Delivery", Proceed. Intern. Symp. Control. Rel. Bioactive. Mater., 1992, 19: 102-103.			
192.	Saffran et al. "A Model for the Study of the Oral Administration of Peptide Hormones" Can J Biochem 57 548-553 1979.			
193.	Saffran, M. et al, "A New Approach to the Oral Administration of Insulin and Other Peptide Drugs," Science, 1986, 233: 1081-1084.			
194.	Santiago, N. et al, "Oral Immunization of Rats with Influenza Virus M Protein (M1) Microspheres," Proceed. Intern. Symp. Cont. Rel. Bioactive. Mater., 1992, 19: 116-117.			
195.	Savva et al., "Effect of PEG Homopolymer and Grafted Amphiphilic PEG-Palmityl on the Thermotropic Phase Behavior of 1,2-Dipalmitoyl-SN-Glycero-3-Phosphocholine Bilayer," Journal of Liposome Research, 9(3): 357-365 (1999).			
196.	Shichiri et al.; "Enteral Absorption of Water-in-Oil-in-Water Insulin Emulsions in Rabbits" Diabetologia 10 317-321 (1974).			
197.	Szeleifer, I. et al., "Spontaneous Liposome Formation Induced by Grafted Poly(Ethylene Oxide) Layers: Theoretical Prediction and Experimental Verification," Proceedings of the National Academy of Sciences of the United States of America, 95(3): 1032-1037 (Feb. 3, 1998).			
198.	Taniguchi, T. et al, "Synthesis of Acyl-Lysozyme and Improvement of its Lymphatic Transport Following Small Intestinal Administration in Rats" Proceed. Intern. Symp. Control. Rel. Bioactiv. Mater., 1992, 19: 104-105.			
199.	Tyle, Praveen, "Iontophoretic Devices for Drug Delivery," Pharmaceutical Research 3(6): 318-326 (1986).			

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 \*EXAMINER

DATE CONSIDERED

Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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